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REMARKS

Favorable reconsideration of this application as presently amended is respectfully requested. Claims 1-7, 9-27, 46 and 47 are pending. No new matter is added.

The above amendments to the specification are identical to the amendments proposed in Applicants' November 15, 2002 Amendment.

Support for the amendments to the specification is found in the specification at page 14, lines 6-10 where it is stated the preferred types of flow cytometers for use in the present invention are described in U.S. Patent Nos. 5,895,764; 5,824,269; 5,395,588; 4,661,913; the entire contents and disclosures of which were incorporated by reference. In particular, the two paragraphs inserted after page 14, line 16 are taken verbatim from U.S. Patent No. 5,395,588 at column 1, lines 28-59, and are directed to describing the operation of flow cytometers of the type that may be used in the flow cytometry apparatus of claim 1. Therefore, the above amendments to the specification do not add new matter.

The Examiner is thanked for indicating the previous rejection of claims 9, 10, 26, 46 and 47 under 35 U.S.C. § 112, second paragraph is withdrawn. The Examiner is thanked for indicating the previous rejection of claims 1-3, 5, 7, 9-12, 15-19 and 26-27 under 35 U.S.C. § 102(b) as being anticipated by Saros *et al.* (U.S. Patent No. 4,853,336) is withdrawn in light of Applicants' arguments. The Examiner is thanked for indicating the previous rejection of claims 4, 6, 13, 14, 20-24, 46 and 47 under 35 U.S.C. § 103(a) as being unpatentable over Saros *et al.* in view of Kercso *et al.* (U.S. Patent No. 6,132,685) is withdrawn in light of Applicants' arguments. The Examiner is thanked for indicating the previous rejection of claim 25 under 35 U.S.C. § 103(a) as being unpatentable over Saros *et al.* in view of Kercso *et al.* and in further view of Farrell *et al.* (U.S. Patent No. 5,788,927) is withdrawn in light of Applicants' arguments.

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Based on paragraph 6 of the Office Action, claims 1-7, 9-27, 46 and 47 stand rejected under 35 U.S.C. § 112, first paragraph. This rejection is improper for the reasons set forth below and should be withdrawn.

Incorporation by reference of "essential material" is permissible under current United States Patent and Trademark practice when the reference is to a (1) U.S. Patent, (2) U.S. Patent Application or Patent Application Publication, or (3) pending U.S. application. See Manual of Patent Examining Practice § 608.01(p)(I)(A) (8th ed. 2001); see e.g., Quaker City Gear Works, Inc. v. Skil Corp., 223 U.S.P.Q. 1161, 1167 (Fed. Cir. 1984) (requiring essential material to be incorporated by reference to a U.S. patent); Ernsthausen v. Nakayama, 1 U.S.P.Q.2d 1539, 1548 (B.P.A.I. 1985) (stating that a U.S. patent or application may incorporate essential material) aff'd 809 F.2d 787 (Fed. Cir. 1986)(unpublished).

Applicants have amended the specification to include two paragraphs from U.S. Patent No. 5,395,588 to North, Jr. *et al.* (North Patent). Applicants have properly incorporated by reference the North Patent by clearly identifying the patent on page 14, lines 7-10 of the specification. Therefore, Applicant's have properly incorporated by reference into the present application the material from the North Patent, set forth in the Amendments to the Specification section in Applicants' November 15, 2002 Amendment and in the present Amendment, by incorporating by reference a portion of a U.S. Patent, namely North '588.

With respect to the present application, the Office Action on page 4 sets forth the following inappropriate standard that "incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper." See MPEP § 608.01(p)(I)(A). This inappropriate standard is inapplicable to the present case, because Applicant's have incorporated material by reference to a U.S. Patent, as permitted under Section 608.01(p)(I)(A) of the MPEP. Furthermore, the requirement set forth in the Office Action on page 4 that Applicants must provide

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an affidavit or declaration to support an amendment to include the material
~~incorporate by reference, is not applicable to the present case.~~

Based on paragraph 7 of the Office, Action, claims 1-7, 9-27, 46 and 47 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification, while being enabling for use of parameter controlled separation gas in a compatible flow cytometric device, does not reasonably provide enablement for the use of any separation gas introduced into any flow cytometric device. This rejection is improper and should be withdrawn for the reasons set forth below.

With respect to claim 1, claim 1 claims “[a] flow cytometry apparatus for the detection of particles from a plurality of samples comprising: means for moving the plurality of samples comprising particles from a plurality of respective source wells into a fluid flow stream, said means for moving the plurality of samples comprising a pump; means for introducing a separation gas between each of said plurality of samples in said fluid flow stream; and a flow cytometer for hydrodynamically focusing said fluid flow stream and selectively analyzing said particles in each of said plurality of samples as said fluid flow stream passes through said flow cytometer.”

With respect claim 1, the specification has described the subject matter in such a way as to convey to one reasonable skilled in the art that at the time the present application was filed that Applicants had possession of the claimed invention. Support for the recitation in claim 1 of “a flow cytometry apparatus for the detection of particles from a plurality of samples,” is found in the specification on page 1, line 21; page 2, lines 17-22; page 4, lines 17-18; page 5, line 20 to page 6, line 2; page 9, lines 1-10; page 9, line 12 to page 10, line 13; and in FIG. 1A, as well as elsewhere through the specification, figures and originally filed claims. Support for the recitation in claim 1 of “means for moving the plurality of samples comprising particles from a plurality of respective source wells into a fluid flow stream, the means for moving the plurality of samples comprising a pump,” is found in the specification

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on page 2, lines 17-22; page 5, line 20 to page 6, line 2; page 7, lines 18-26; page 9, line 12 to page 10, line 13; page 12, lines 12-25; page 13, lines 18-24; page 14, lines 25-30; and in FIG. 1A, as well as elsewhere through the specification, figures and originally filed claims. Support for the recitation in claim 1 of “means for introducing a separation gas between each of the plurality of samples in the fluid flow stream,” is found in the specification on page 2, lines 17-22; page 6, lines 13-20; page 7, lines 18-26; page 9, lines 1-10; page 9, line 12 to page 10, line 13; page 10, line 15-page 11, line 6; and in FIGs. 1B, 1C, as well as elsewhere through the specification, figures and originally filed claims. Applicants have properly described subject matter in the specification as required by 35 U.S.C. § 112, first paragraph. Therefore, claim 1 is enabled and the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, is improper.

With respect to the comments in the Office Action at pages 4-8 with respect to the potential use of “any separation gas introduced into any flow cytometric device” (see Office Action, p. 4), the Board of Patent Appeals has held:

Claims are addressed to the person of average skill in the particular art. Compliance with 112 must be adjudged from that perspective, not in a vacuum. It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. *See Ex Parte Cole*, 223 USPQ 94, 95-96 (PTO Bd. App. 1983).

The present application gives considerable guidance to a person of ordinary skill in the art as to which types of separation gas are suitable for use in the flow cytometry apparatus of claim 1. For example, in defining the term “separation gas” the specification states: “For the purposes of the present invention, the term “separation gas” refers to any gas such as air, an inert gas, or fluid *etc.* that can be used to form a gas bubble or immiscible fluid between adjacent samples or between a sample and a buffer fluid. An immiscible fluid is a fluid that will not substantially mix with and contaminate a sample.” (*See* specification, p. 6, lines 13-15). The Office Action has given no reason why the description of separation gas in the specification would not

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allow a person of ordinary skill in the art to determine which separation gases are suitable for the purposes of the claimed invention.

Similarly, the present application has described a number of suitable flow cytometry apparatuses suitable for use with the flow cytometry apparatus of claim 1. As stated in the application, "Various types of flow cytometers may be used with the flow cytometry apparatus of the present invention. Preferred types of flow cytometers are described in U.S. Patent Nos. 5,895,764; 5,824,269; 5,395,588; 4,661,913." (*See* specification, p. 14, lines 8-10). The Office Action has given no reason why the description of the use of the flow cytometer in the working Example (*see* specification, pp. 15-16) and the description of the flow cytometers in the four cited patents would not allow a person of ordinary skill in the art to determine which flow cytometer to use in the apparatus of claim 1.

For at least the above reasons, claim 1 is enabled so that one skilled in the art would be able to make and use the claimed features of claim 1 and the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, is improper and should be withdrawn.

With respect to claims 2-7, 9-27, 46 and 47, these claims are dependent on claim 1, either directly or indirectly, and, therefore, with respect to the features claims 2-7, 9-27, 46 and 47 have in common with claim 1, are enabled for the reasons discussed above with respect to claim 1. With respect to the additional features of claims 2-7, 9-27, 46 and 47, the Office Action has cited no grounds as to why the additional features of claims 2-7, 9-27, 46 and 47 are not enabled. Therefore, claims 2-7, 9-27, 46 and 47 are enabled and the rejection of claims 2-7, 9-27, 46 and 47 set forth in paragraph 7 of the Office Action is improper and should be withdrawn.

Furthermore, with respect to claim 9, the grounds of rejection in paragraph 4 is also *prima facie* improper, because claim 9 claims that the separation gas is air, and therefore, claim 9 does not even claim the "use of any separation gas." Therefore, the

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rejection of claim 9 set forth in paragraph 7 of the Office Action is improper for this additional reason and should be withdrawn.

With respect to the prior art, the Office Action states “the prior art of record fails to disclose a flow cytometry apparatus for hydrodynamic focusing of flow streams for analysis of particles in a plurality of samples which are separated by a separation gas.” (See OA, page 5). Applicants strongly agree with the Office Action that the prior art of records fails to disclose a flow cytometry apparatus for hydrodynamic focusing of flow streams for analysis of particles in a plurality of samples which are separated by a separation gas.

Claims 1-3, 5, 7, 9-12, 15-19 and 26-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Saros *et al.* in view of Weigl *et al.* (U.S. Patent No. 6,159,739). This rejection is respectfully traversed.

With respect to claim 1, claim 1 claims a flow cytometry apparatus for the detection of particles from a plurality of samples comprising: means for moving the plurality of samples comprising particles from a plurality of respective source wells into a fluid flow stream, the means for moving the plurality of samples comprising a pump; means for introducing a separation gas between each of the plurality of samples in the fluid flow stream; and a flow cytometer for hydrodynamically focusing the fluid flow stream and selectively analyzing the particles in each of the plurality of samples as the fluid flow stream passes through the flow cytometer. However, the Office Actions affirms “the prior art of record fails to disclose a flow cytometry apparatus for hydrodynamic focusing of flow streams for analysis of particles in a plurality of samples which are separated by a separation gas.” (See Office Action, p. 5). Therefore, the Office Action effectively states the cited prior art does not teach claim 1’s feature of a flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas. Furthermore, the Office Action also indicates that the prior art does not

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suggest claim 1's feature of a flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas, because the Office Action states "there is specific teaching in the flow cytometry art against air bubbles in fluid flow streams wherein optimally, the bubbles would be removed from samples prior to injection into fluid flow tubing." (See Office Action, p. 7). Therefore, the above-cited statements in the Office Action indicate that the rejection of claim 1 based on Saros *et al.* in view of Weigl *et al.* is improper and should be withdrawn, because the Office Action has effectively stated that claim 1 is nonobvious over the prior art of record.

In addition, Saros *et al.* is cited for teaching "a single tubing continuous flow analyzer system in which a successive plurality of samples containing biomaterial and test compounds are separate by immiscible segments which permit delayed on-line mixing of the components in the mixtures." (See Office Action, p. 9). However, as stated by the Office Action, Saros *et al.*, does not "disclosure a flow cytometer for hydrodynamically focusing the fluid stream for analysis of particles in the samples as the fluid stream passes through the flow cytometer." (See Office Action, p. 10). Nowhere does Saros *et al.* teach or suggest any means for hydrodynamically focusing a fluid flow stream, much less a flow cytometer for focusing a fluid flow stream. Therefore, Saros *et al.* cannot teach or suggest claim 1's feature of a flow cytometry apparatus for hydrodynamically focusing a fluid flow streams for analysis of particles in a plurality of samples which are separated by a separation gas.

Weigl *et al.* is cited for teaching "a flow module for reproducibly focusing particles into the measurement zone of a flow cytometer." (See Office Action, p.10). However, the Office Action states, "there is specific teaching in the flow cytometry art against air bubbles in fluid flow streams wherein optimally, the bubbles would be removed from samples prior to injection into fluid flow tubing." (See Office Action, p. 7). Therefore, according to the Office Action, there is no motivation for combining

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Weigl *et al.* with Saros *et al.*, and the combination of Weigl *et al.* with Saros *et al.* is improper.

In addition, the Office Action has not cited any evidence in any of the cited prior art providing a motivation to combine in Saros *et al.* to combine the teachings of the teachings of Weigl *et al.* with the teaching of Saros *et al.* Instead the Office Action states that it would be obvious to combine the teachings of Weigl *et al.* with the teachings of Saros *et al.* and does not provide any motivation in Saros *et al.* for the combination. The statement in the Office Action at page 11 that “[o]ne of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate flow cytometric modules as used by Weigl into the flow analyzer taught by Saros to create a versatile flow cytometric system capable of analyzing various sample particles” is a mere conclusory statement and is unsupported by any cited portion of Weigl *et al.* or Saros *et al.* and is contradicted by the Office Action’s own statements that the prior art teaches away from such a combination. (See Office Action, p. 7). Therefore, the Office Action has not set forth a proper rejection under 35 U.S.C. § 103(a), and the rejection of claim 1 based on Saros *et al.* and Weigl *et al.* should be withdrawn as improper.

For the above reasons, the rejection of claim 1 based on the combination of Weigl *et al.* with Saros *et al.* is improper and claim 1 is patentable over the combination of Weigl *et al.* with Saros *et al.*

With respect to claims 2, 3, 5, 7, 9-12, 15-19 and 26-27, claims 2, 3, 5, 7, 9-12, 15-19 and 26-27 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 2, 3, 5, 7, 9-12, 15-19 and 26-27 are patentable over Saros *et al.* in view of Weigl *et al.*, and the rejection under 35 U.S.C. § 103(a) is improper for at least the reasons discussed above with respect to claim 1.

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Claims 4, 6, 13-14, 20-24, 46 and 47 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Saros *et al.* in view of Weigl *et al.* and in further view of Kercso *et al.* (U.S. Patent No. 6,132,685). This rejection is respectively obviated with respect to the argument presented below.

With respect to claims 4, 6, 13-14, 20-24, 46 and 47, claims 4, 6, 13-14, 20-24, 46 and 47 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1, including claim 1's feature of a flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas, as well as other patentable features. Therefore, claims 4, 6, 13-14, 20-24, 46 and 47 are patentable over the combination of Weigl *et al.* with Saros *et al.* for at least the reasons discussed above with respect to claim 1.

Kercso *et al.* is only cited for teaching analyzing a large number of samples contained in standard multiwell microtiter plates. In addition, Kercso *et al.* is cited for using microfluidic flow channels that are made of PVC. However, Kercso *et al.* cannot remedy the deficiencies in Saros *et al.* and Weigl *et al.* with respect to failing to teach the feature of claims 4, 6, 13-14, 20-24, 46 and 47 of a flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas. Therefore, claims 4, 6, 13-14, 20-24, 46 and 47 are patentable over the combination of Kercso *et al.* with Saros *et al.* and Weigl *et al.*

Claim 25 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Saros *et al.* in view of Weigl *et al.* and in further view of Kercso *et al.* and in further view of Farrell *et al.* (U.S. Patent No. 5,788,927). This rejection is respectively traversed.

With respect to claim 25, claim 25 depends claim 20, and, accordingly, includes all of the patentable features of claim 20, including claim 20's feature of a

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flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas as well as other patentable features. Therefore, 25 is patentable over the combination of Kercso *et al.* with Saros *et al.* and Weigl *et al.* for at least the reasons discussed above with respect to claim 20.

Farrell *et al.* is only cited for teaching a flow analyzer system that incorporates an automated samples having a sealed sample source that is inverted and moves relative to the probe of the autosampler. However, Farrell *et al.* cannot remedy the deficiencies of the combination of Kercso *et al.* with Saros *et al.* and Weigl *et al.* with respect to for failing to with respect to failing to teach the feature of claim 25 of a flow cytometry apparatus for hydrodynamically focusing a fluid flow stream for analysis of particles in a plurality of samples which are separated by a separation gas. Therefore, claim 25 is patentable over the combination of Farrell *et al.* with Saros *et al.*, Weigl *et al.* and Kercso *et al.*

In addition, with respect to claims 1-7, 9-27, 46 and 47, these claims have been rejected on the basis of facts within the personal knowledge of the Examiner. At page 11, the Office Action states: "One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate flow cytometric measurement modules as used by Weigl in the flow analyzer taught by Saros to create a versatile flow cytometric system capable of analyzing various sample particles because Weigl specifically taught widespread application of flow cytometric measurement modules in analyzing widespread application of flow cytometric measurement modules in analyzing microscopic particles for determining physical and chemical properties in the fields of hematology, immunology, genetics, parasitology, oncology, *etc.*" However, the Examiner has cited no portion of Saros *et al.* or Weigl *et al.* supporting the conclusory statement quoted above. Furthermore, the Examiner has provided no reason for ignoring the Examiner's own admission that "there is specific teaching in the flow cytometry art against air bubbles in fluid flow streams wherein optimally, the bubbles

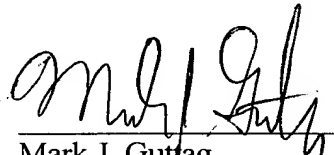
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would be removed from samples prior to injection into fluid flow tubing.” (See Office Action, p. 7). Therefore, claims 1-7, 9-27, 46 and 47, have been rejected on the basis of facts within the personal knowledge of the Examiner, and, accordingly, under 37 C.F.R. § 1.104(d)(2) the Applicants hereby request that the Examiner provide an affidavit supporting the Examiner’s assertion used as a basis for the rejection of claims 1-7, 9-27, 46 and 47.

If the Examiner has any questions or concerns regarding the present response, the Examiner is invited to contact Mark J. Guttag at 703-591-2664.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance, and favorable action is respectfully solicited.

Respectfully submitted,


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